# WE CLAIM:

1. A compound selected from the group consisting of:

and

or a pharmaceutically acceptable salt, solvate, clathrate, or prodrug thereof.

2. A composition comprising an effective amount of a compound of formula (I):

$$R_{3} \xrightarrow{\stackrel{R_{2}}{(c)_{1}}} Y \xrightarrow{N} X \xrightarrow{R_{1}} X$$

$$R_{4} \xrightarrow{Z} R_{5}$$

$$(I)$$

wherein .

$$N = \stackrel{R^a}{\swarrow}$$
 $R_1$  is  $R^b$ , aryl, or heteroaryl;

each of  $R_2$  and  $R_4$ , independently, is  $R^c$ , halogen, nitro, cyano, isothionitro,  $SR^c$ , or  $OR^c$ ; or  $R_2$  and  $R_4$ , taken together, is carbonyl.

R<sub>3</sub> is R<sup>c</sup>, alkenyl, alkynyl, OR<sup>c</sup>, OC(O)R<sup>c</sup>, SO<sub>2</sub>R<sup>c</sup>, S(O)R<sup>c</sup>, S(O<sub>2</sub>)NR<sup>c</sup>R<sup>d</sup>, SR<sup>c</sup>, NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>COR<sup>d</sup>, NR<sup>c</sup>C(O)OR<sup>d</sup>, NR<sup>c</sup>C(O)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>SO<sub>2</sub>R<sup>d</sup>, COR<sup>c</sup>, C(O)OR<sup>c</sup>, or C(O)NR<sup>c</sup>R<sup>d</sup>;

R<sub>5</sub> is H or alkyl;

n is 0, 1, 2, 3, 4, 5, or 6;

X is O, S, S(O), S(O<sub>2</sub>), or  $NR^c$ ;

Y is a covalent bond,  $CH_2$ , C(O),  $C=N-R^c$ ,  $C=N-OR^c$ ,  $C=N-SR^c$ , O, S, S(O),  $S(O_2)$ , or  $NR^c$ ;

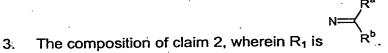
Z is N or CH;

one of U and V is N, and the other is CRc; and

W is O, S, S(O), S(O<sub>2</sub>),  $NR^c$ , or  $NC(O)R^c$ ;

in which each of R<sup>a</sup> and R<sup>b</sup>, independently, is H, alkyl, aryl, heteroaryl; and each of R<sup>c</sup> and R<sup>d</sup>, independently, is H, alkyl, aryl, heteroaryl, cyclyl, heterocyclyl, or alkylcarbonyl

or a pharmaceutically acceptable salt, solvate, clathrate, or prodrug thereof.



- 4. The composition of claim 3, wherein U is N and V is CH.
- 5. The composition of claim 3, wherein Z is N and W is O.
- 6. The composition of claim 3, wherein X is NR<sup>c</sup>.
- 7. The composition of claim 3, wherein Y is O, S, or CH<sub>2</sub>, and n is 0, 1, 2, 3, or 4
- 8. The composition of claim 7, wherein  $R_3$  is anyl or heteroaryl.

- 9. The composition of claim 7, wherein  $R_3$  is  $OR^c$ ,  $SR^c$ ,  $C(O)OR^c$ , or  $C(O)NR^cR^d$ .
- 10. The composition of claim 7, wherein R<sub>3</sub> is

$$R^{e}$$
  $A$  or  $R^{e}$   $A$ 

wherein

each of A and A', independently, is O, S, or NH; each of  $R^e$  and  $R^f$ , independently is H, alkyl, aryl, or heteroaryl; and m is 1 or 2.

11. The composition of claim 3, wherein one of R<sup>a</sup> and R<sup>b</sup> is

$$\mathbb{R}^{\mathbf{B}} = \mathbb{R}^{\mathbf{B}} \quad \text{or} \quad \mathbb{R}^{\mathbf{B}} = \mathbb{R}^{\mathbf{B}}$$

in which

B is NR<sup>i</sup>, O, or S;

B' is N or CRi;

R<sup>9</sup> is H, halogen, CN, alkyl, cyclyl, alkyloxy, alkylcarbonyl, alkyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, hydroxyalkyl, alkylamino, or alkylaminocarbonyl;

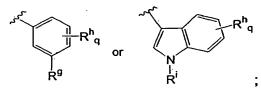
R<sup>h</sup> is H, halogen, NO<sub>2</sub>, CN, alkyl, aryl, heteroaryl, OR<sup>c</sup>, OC(O)R<sup>c</sup>, SO<sub>2</sub>R<sup>c</sup>, S(O)R<sup>c</sup>, S(O<sub>2</sub>)NR<sup>c</sup>R<sup>d</sup>, SR<sup>c</sup>, NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>COR<sup>d</sup>, NR<sup>c</sup>C(O)OR<sup>d</sup>, NR<sup>c</sup>C(O)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>SO<sub>2</sub>R<sup>d</sup>, COR<sup>c</sup>, C(O)OR<sup>c</sup>, or C(O)NR<sup>c</sup>R<sup>d</sup>;

R<sup>i</sup> is H, alkyl, or alkylcarbonyl;

p is 0, 1, or 2; and

q is 0, 1, 2, 3, or 4.

12. The composition of claim 11, wherein one of Ra and Rb is



in which R<sup>g</sup>, R<sup>h</sup>, R<sup>i</sup>, and q are as defined in claim 11; and the other of R<sup>a</sup> and R<sup>b</sup> is H or alkyl.

- 13. The composition of claim 12, wherein
- R<sup>g</sup> is H, methyl, ethyl, propyl, cyclopropyl, methoxy, ethoxy, methoxycarbonyl, methylaminocarbonyl or halogen;
- $R^h$  is F, CI, CN, methyl, methoxy, ethoxy, OC(O)CH<sub>3</sub>, OC(O)C<sub>2</sub>H<sub>5</sub>, C(O)OH, C(O)OC<sub>2</sub>H<sub>5</sub>, C(O)NH<sub>2</sub>, NHC(O)CH<sub>3</sub>, or S(O<sub>2</sub>)NH<sub>2</sub>;
- R<sup>i</sup> is H, methyl, ethyl, or acetyl, and q is 0, 1, or 2.
- 14. The composition of claim 13, wherein U is N, V is CH, Z is N, and W is O.
- 15. The composition of claim 14, wherein X is NR<sup>c</sup>; and R<sup>c</sup> is H, methyl, ethyl, or acetyl.
- 16. The composition of claim 15, wherein Y is O, S, or CH<sub>2</sub>; and n is 0, 1, 2, 3, or 4.
- 17. The composition of claim 16, wherein R<sub>3</sub> is R<sup>c</sup>, OR<sup>c</sup>, SR<sup>c</sup>, C(O)OR<sup>c</sup>, or C(O)NR<sup>c</sup>R<sup>d</sup>.
- 18. The composition of claim 17, wherein R<sub>3</sub> aryl, heteroaryl, hydroxyl, alkyloxy, or heteroaryloxy.
- 19. The composition of claim 2, wherein R<sub>1</sub> is aryl or heteroaryl.
- 20. The composition of claim 19, wherein R<sub>1</sub> is

wherein

D is O, S, or NR<sup>m</sup>;

Ri is benzo, halogen, CN, hydroxyl, alkyl, aryl, heteroaryl, alkoxyl, aryloxyl, or heteroaryloxyl;

R<sup>m</sup> is H, alkyl, or alkylcarbonyl; and r is 0, 1, or 2.

- 21. The composition of claim 20, wherein X is NR<sup>c</sup>; and R<sup>c</sup> is H, methyl, ethyl, or acetyl.
- 22. The composition of claim 21, wherein U is N, V is CH, Z is N, and W is O.
- 23. The composition of claim 22, wherein Y is O, S, or  $CH_2$ ; and n is 0, 1, 2, 3, or 4.
- 24. The composition of claim 23, wherein  $R_3$  is aryl or heteroaryl.
- 25. The composition of claim 23, wherein  $R_3$  is  $OR^c$ ,  $SR^c$ ,  $C(O)OR^c$ , or  $C(O)NR^cR^d$ .
- 26. The composition of claim 23, wherein R<sub>3</sub> is

$$R^{e}$$
  $A$  or  $R^{e}$   $A$ 

wherein

each of A and A', independently, is O, S, or NH; each of R<sup>e</sup> and R<sup>f</sup>, independently is H, alkyl, aryl, or heteroaryl; and m is 1 or 2.

27. The compound of claim 23, wherein  $R_1$  is

wherein R<sup>m</sup> is H, alkyl, or alkylcarbonyl; R<sup>j</sup> is methyl, ethyl, propyl, or benzo; and r is 1 or 2.

28. The composition of claim 2, wherein

$$N = \begin{pmatrix} R^a \\ R_1 \text{ is } R^b \end{pmatrix}$$

each of R<sub>2</sub> and R<sub>4</sub> is H;

R<sub>3</sub> is H, alkyl, aryl, heteroaryl, cyclyl, heterocyclyl, alkyloxycarbonyl, alkylaminocarbonyl, or alkylcarbonyl; and X is NR<sup>c</sup>.

- 29. The composition of claim 28, wherein X is NH.
- 30. The composition of claim 28, wherein one of R<sup>a</sup> and R<sup>b</sup> is H or alkyl; and the other is aryl or heteroaryl optionally substituted with R<sup>g</sup> and R<sup>h</sup><sub>q</sub>; R<sup>g</sup> being halogen, CN, alkyl, alkyloxy, alkylcarbonyl, alkyloxycarbonyl, aryloxycarbonyl, heteroaryloxycarbonyl, hydroxyalkyl, alkylamino, or alkylaminocarbonyl; R<sup>h</sup> being halogen, CN, hydroxyl, alkyl, aryl, heteroaryl, alkoxyl, aryloxyl, or heteroaryloxyl; and q being 0, 1, 2, 3, or 4.
- 31. The composition of claim 29, wherein one of R<sup>a</sup> and R<sup>b</sup> is H or alkyl; and the other is

#### wherein

R<sup>9</sup> is H, alkyl, alkoxyl, methoxycarbonyl, methylaminocarbonyl, or halogen; R<sup>h</sup> is halogen, CN, hydroxyl, alkyl, aryl, heteroaryl, alkoxyl, aryloxyl, or heteroaryloxyl; and q is 0, 1, 2, 3, or 4.

- 32. The composition of claim 28, wherein U is N, V is CH, Z is N, and W is O.
- 33. The composition of claim 32, wherein R<sub>3</sub> is heteroaryl or heterocyclyl.
- 34. The composition of claim 33, wherein R<sub>3</sub> is pyridinyl.
- 35. The composition of claim 33, wherein  $R_3$  is 1-oxy-pyridinyl.
- 36. The composition of claim 33, wherein R<sub>3</sub> is 1*H*-pyridin-2-one.
- 37. The composition of claim 33, wherein n is 2, and Y is O.
- 38. The composition of claim 37, wherein X is NH.
- 39. The composition of claim 38, wherein one of  $R^a$  and  $R^b$  is H or alkyl; and the other is

#### wherein

R<sup>9</sup> is H, alkyl, alkoxyl, methoxycarbonyl, methylaminocarbonyl, or halogen; R<sup>h</sup> is halogen, CN, hydroxyl, alkyl, aryl, heteroaryl, alkoxyl, aryloxyl, or heteroaryloxyl; and q is 0, 1, 2, 3, or 4.

40. The composition of claim 38, wherein one of R<sup>a</sup> and R<sup>b</sup> is H; and the other is



in which R<sup>9</sup> is as defined in claim 39.

- 41. The composition of claim 2, wherein the compound is:
- N-{2-[3-(3,4-dimethoxy-phenyl)-propyl]-6-morpholin-4-yl-pyrimidin-4-yl}-N'- (1H-indol-3-ylmethylene)-hydrazine,
- N-(2-n-butoxy-6-morpholin-4-yl-pyrimidin-4-yl)-N'-(1H-indol-3-ylmethylene)-hydrazine,
- N-(2-(4-hydroxybutyl)-6-morpholin-4-yl-pyrimidin-4-yl)-N'-(1H-indol-3-ylmethylene)-hydrazine,
- N-[2-(2-[1,3]dioxan-2-yl-ethyl)-6-morpholin-4-yl-pyrimidin-4-yl]-N'-(1H-indol-3-yl methylene)-hydrazine
- N-(1H-indol-3-ylmethylene)-N'-[2-(3-methoxy-propyl)-6-morpholin-4-yl-pyrimidin -4-yl]-hydrazine,
- 3-{4-[N'-(1H-indol-3-ylmethylene)-hydrazino]-6-morpholin-4-yl-pyrimidin-2-ylsulfanyl}-propan-1-ol,
- 3-{2-[N'-(1H-indol-3-ylmethylene)-hydrazino]-6-morpholin-4-yl-pyrimidin-4-ylsulfanyl}-propan-1-ol,
- N-[2-(2,2-dimethyl-[1,3]dioxolan-4-ylmethoxy)-6-morpholin-4-yl-pyrimidin-4-yl]-N'-(1H-indol-3-ylmethylene)-hydrazine,
- N-{2-[2-(3,4-dimethoxy-phenyl)-ethoxy]-6-morpholin-4-yl-pyrimidin-4-yl}-N'- (1H-indol-3-ylmethylene)-hydrazine,
- N-(1H-indol-3-ylmethylene)-N'-[6-morpholin-4-yl-2-(2-pyridin-2-yl-ethoxy)-pyrimidin-4-yl]-hydrazine,
- N-(1H-indol-3-ylmethylene)-N'-[6-morpholin-4-yl-2-(3-pyridin-2-yl-propyl)-pyrimidin-4-yl]-hydrazine,
- N-(3-methyl-benzylidene)-N'-[6-morpholin-4-yl-2-(2-pyridin-2-yl-ethoxy)-pyrimidin-4-yl]-hydrazine,
- N-(3-ethyl-benzylidene)-N'-[6-morpholin-4-yl-2-(2-pyridin-2-yl-ethoxy)-pyrimidin-4-yl]-hydrazine,

- N-(3-methyl-benzylidene)-N'-[6-morpholin-4-yl-2-(3-pyridin-2-yl-propyl)-pyrimidin-4-yl]-hydrazine,
- N-[6-morpholin-4-yl-2-(2-pyridin-2-yl-ethoxy)-pyrimidin-4-yl]-N'-(1-m-tolyl-ethylidene)-hydrazine,
- N-[1-(1H-indol-3-yl)-ethylidene]-N'-[6-morpholin-4-yl-2-(2-pyridin-2-yl-ethoxy)-pyrimidin-4-yl]-hydrazine,
- 3-methyl-benzaldehyde
  - O-[6-morpholin-4-yl-2-(2-pyridin-2-yl-ethoxy)-pyrimidin-4-yl]-oxime,
- 1H-indole-3-carbaldehyde
  - O-[6-morpholin-4-yl-2-(2-pyridin-2-yl-ethoxy)-pyrimidin-4-yl]-oxime,
- N-(1H-indol-3-ylmethylene)-N'-{6-morpholin-4-yl-2-[2-(pyridin-3-yloxy)-ethoxy]-pyrimidin-4-yl}-hydrazine,
- N-(3-methyl-benzylidene)-N'-{6-morpholin-4-yl-2-[2-(pyridin-3-yloxy)-ethoxy]-pyrimidin-4-yl}-hydrazine,
- butyl-{4-[N'-(1H-indol-3-ylmethylene)-hydrazino]-6-morpholin-4-yl-pyrimidin-2-yl}-amine,
- N-(3-methyl-benzylidene)-N'-[6-morpholin-4-yl-2-(pyridin-3-yloxy)-pyrimidin-4-yl]-hydrazine,
- N-(3-methylbenzlidene)-N'-(5-methyl-6-morpholin-4-yl-2-phenylpyrimidin-4-yl)hydrazine,
- N-(3-methyl-benzylidene)-N'-(2-phenyl-6-thiomorpholin-4-yl-pyrimidin-4-yl)-hydrazine,
- (2,3-dimethyl-1H-indole-5-yl)-{6-morpholin-4-yl-2-[2-(pyridin-3-yloxy)-ethoxy]-pyrimidin-4-yl}-amine,
- (2,3-dimethyl-1H-indole-5-yl)-{4-morpholin-4-yl-6-[2-(pyridin-3-yloxy)-ethoxy]-pyrimidin-2-yl}-amine,
- 3-{4-[N'-(3-methyl-benzylidene)-hydrazino]-6-morpholin-4-yl-pyrimidin-2-yl}propionic acid ethyl ester,
- N-(3-methyl-benzylidene)-N'-{6-morpholin-4-yl-2-[2-(1-oxy-pyridin-2-yl)-ethoxy]-pyrimidin-4-yl}-hydrazine,
- 1-(2-{4-[N'-(3-methyl-benzylidene)-hydrazino]-6-morpholin-4-yl-pyrimidin-2-yloxy}-ethyl)-1H-pyridin-2-one,

- N-(3-iodo-benzylidene)-N'-[6-morpholin-4-yl-2-(2-pyridin-2-yl-ethoxy)-pyrimidin-4-yl]-hydrazine,
- N-(3-fluoro-benzylidene)-N'-[6-morpholin-4-yl-2-(2-pyridin-2-yl-ethoxy)-pyrimidin-4-yl]-hydrazine,
- N-(3-chloro-benzylidene)-N'-[6-morpholin-4-yl-2-(2-pyridin-2-yl-ethoxy)-pyrimidin-4-yl]-hydrazine,
- N-(3-bromo-benzylidene)-N'-[6-morpholin-4-yl-2-(2-pyridin-2-yl-ethoxy)-pyrimidin-4-yl]-hydrazine,
- 3-{[6-morpholin-4-yl-2-(2-pyridin-2-yl-ethoxy)-pyrimidin-4-yl]-hydrazonomethyl}-benzoic acid methyl ester,
- 1-(2-{4-[N'-(3-iodo-benzylidene)-hydrazino]-6-morpholin-4-yl-pyrimidin-2-yloxy}-ethyl)-1H-pyridin-2-one,
- 3-{[6-morpholin-4-yl-2-(2-pyridin-2-yl-ethoxy)-pyrimidin-4-yl]-hydrazonomethyl}-benzoic acid N-methyl amide, or
- (3-{[6-morpholin-4-yl-2-(2-pyridin-2-yl-ethoxy)-pyrimidin-4-yl]-hydrazonomethyl}-phenyl)-methanol,
- N,N-Diethyl-4-{4-[N"-(3-methyl-benzylidene)-hydrazino]-6-morpholin-4-yl-pyrimidin-2-yl}-butyramide,
- 4-{4-[N'-(3-Methyl-benzylidene)-hydrazino]-6-morpholin-4-yl-pyrimidin-2-yl}-1-(4-methyl-piperazin-1-yl)-butan-1-one,
- 4-{4-[N'-(3-Methyl-benzylidene)-hydrazino]-6-morpholin-4-yl-pyrimidin-2-yl}-N-pyridin-4-ylmethyl-butyramide,
- 4-{4-[N'-(3-Methyl-benzylidene)-hydrazino]-6-morpholin-4-yl-pyrimidin-2-yl}-N-pyridin-4-yl-butyramide.
- 2-{4-[N'-(3-Methyl-benzylidene)-hydrazino]-6-morpholin-4-yl-pyrimidin-2-yloxy}-1-pyridin-2-yl-ethanol
- 6-(2-{4-[N'-(3-Methyl-benzylidene)-hydrazino]-6-morpholin-4-yl-pyrimidin-2-yloxy}-ethyl)-pyridin-3-ol
- 6-(2-{4-[N'-(3-Hydroxymethyl-benzylidene)-hydrazino]-6-morpholin-4-yl-pyrimidin-2-yloxy}-ethyl)-pyridin-3-ol
- 42. A method for treating or preventing a disorder associated with excessive bone loss, the method comprising administering to a patient in need thereof

a compound according to claim 1, a composition comprising an effective amount of a compound according to claim 1, a compound according to formula (I) as described in any one of claims 2-41, or a composition according to any one of claims 2-41.

- 43. The method according to claim 42, wherein the disorder is selected from the group consisting of periodontal disease, non-malignant bone disorders (such as osteoporosis, Paget's disease of bone, osteogenesis imperfecta, fibrous dysplasia, and primary hyperparathyroidism) estrogen deficiency, inflammatory bone loss, bone malignancy, arthritis, osteopetrosis, and certain cancer-related disorders (such as hypercalcemia of malignancy (HCM), osteolytic bone lesions of multiple myeloma and osteolytic bone metastases of breast cancer and other metastatic cancers)
- 44. The method according to claim 42 or 43, the method further comprising administering another therapeutic agent.
- 45. The method according to claim 44, wherein the other therapeutic agent is selected from the group consisting of: anti-resorptive agents, non-steroidal anti-inflammatory agents, steroids, and analgesics.
- 46. The method according to claim 45, wherein the anti-resporptive agent is selected from the group consisting of progestins, polyphosphonates, bisphosphonate(s), estrogen agonists/antagonists, estrogen,estrogen/progestin combinations, and estrogen derivatives.
- 47. The method according to claim 46, wherein the estrogen derivative is estrone, estriol or  $17\alpha$ ,  $17\beta$ -ethynyl estradiol.
- 48. A method for inhibiting osteoclast formation in a pre-osteoclast cell the method comprising contacting the cell with a compound according to claim 1, a composition comprising an effective amount of a compound according to

claim 1, a compound according to formula (I) as described in any one of claims 2-41, or a composition according to any one of claims 2-41.

## 49. A compound selected from the group consisting of:

or a pharmaceutically acceptable salt, solvate, clathrate, or prodrug thereof.

### 50. A compound of formula (l'):

$$R_3$$
 $R_4$ 
 $R_4$ 
 $R_5$ 
 $R_5$ 
 $R_7$ 
 $R_7$ 

wherein.

 $\begin{array}{c}
R^{\circ} \\
N = \\
R_{1} \text{ is } R^{\circ} \\$ , aryl, or heteroaryl;

each of  $R_2$ ,  $R_4$ , and  $R_5$ , independently, is  $R^c$ , halogen, nitro, nitroso, cyano, azide, isothionitro,  $SR^c$ , or  $OR^c$ ;

R<sub>3</sub> is R<sup>c</sup>, alkenyl, alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, OR<sup>c</sup>, OC(O)R<sup>c</sup>, SO<sub>2</sub>R<sup>c</sup>, S(O)R<sup>c</sup>, S(O<sub>2</sub>)NR<sup>c</sup>R<sup>d</sup>, SR<sup>c</sup>, NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>COR<sup>d</sup>, NR<sup>c</sup>C(O)OR<sup>d</sup>, NR<sup>c</sup>C(O)NR<sup>c</sup>R<sup>d</sup>, NR<sup>c</sup>SO<sub>2</sub>R<sup>d</sup>, COR<sup>c</sup>, C(O)OR<sup>c</sup>, or C(O)NR<sup>c</sup>R<sup>d</sup>;

n is 0, 1, 2, 3, 4, 5, 6, or 7;

X is O, S, S(O), S(O<sub>2</sub>), or  $NR^c$ ;

Y is a covalent bond, CH<sub>2</sub>, C(O), C=N-R<sup>c</sup>, C=N-OR<sup>c</sup>, C=N-SR<sup>c</sup>, O, S, S(O), or S(O<sub>2</sub>);

Z is N; and

W is O, S, S(O), S(O<sub>2</sub>),  $NR^c$ , or  $NC(O)R^c$ ;

in which each of R<sup>a</sup> and R<sup>b</sup>, independently, is H, alkyl, aryl, heteroaryl; and each of R<sup>c</sup> and R<sup>d</sup>, independently, is H, alkyl, or alkylcarbonyl or a pharmaceutically acceptable salt, solvate, clathrate, or prodrug thereof.

51. A composition comprising an effective amount of a compound of formula (I'):

$$R_3$$
 $R_4$ 
 $R_4$ 
 $R_5$ 
 $R_4$ 
 $R_5$ 
 $R_6$ 
 $R_6$ 
 $R_7$ 
 $R_8$ 

wherein

$$R_1$$
 is  $R^b$  , aryl, or heteroaryl;

each of  $R_2$ ,  $R_4$ , and  $R_5$ , independently, is  $R^c$ , halogen, nitro, nitroso, cyano, azide, isothionitro,  $SR^c$ , or  $OR^c$ ;

 $R_3$  is  $R^c$ , alkenyl, alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl,  $OR^c$ ,  $OC(O)R^c$ ,  $SO_2R^c$ ,  $S(O)R^c$ ,  $S(O_2)NR^cR^d$ ,  $SR^c$ ,  $NR^cR^d$ ,  $NR^cCOR^d$ ,  $NR^cC(O)OR^c$ ,  $NR^cC(O)NR^cR^d$ ,  $NR^cSO_2R^d$ ,  $COR^c$ ,  $C(O)OR^c$ , or  $C(O)NR^cR^d$ ;

n is 0, 1, 2, 3, 4, 5, 6, or 7;

X is O, S, S(O), S(O<sub>2</sub>), or  $NR^c$ ;

Y is a covalent bond, CH<sub>2</sub>, C(O), C=N-R<sup>c</sup>, C=N-OR<sup>c</sup>, C=N-SR<sup>c</sup>, O, S, S(O), S(O<sub>2</sub>), or NR<sup>c</sup>,

Z is CH; and

W is O, S, S(O), S(O<sub>2</sub>), NR<sup>c</sup>, or NC(O)R<sup>c</sup>; in which each of R<sup>a</sup> and R<sup>b</sup>, independently, is H, alkyl, aryl, heteroaryl; and each of R<sup>c</sup> and R<sup>d</sup>, independently, is H, alkyl, or alkylcarbonyl or a pharmaceutically acceptable salt, solvate, clathrate, or prodrug thereof.

## 52. A compound selected from the group consisting of:

and

or a pharmaceutically acceptable salt, solvate, clathrate, or prodrug thereof.

# 53. A compound of formula (I"):

$$R_3$$
 $R_4$ 
 $R_4$ 
 $R_5$ 
 $R_5$ 
 $R_1$ 

wherein

 $R_1$  is aryl or heteroaryl; each of  $R_2$  and  $R_4$ , independently, is H, halogen, CN, alkyl,  $OR^a$ , or  $NR^aR^b$ ;

 $R_3 \text{ is H, halogen, CN, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cyclyl,} \\ \text{heterocyclyl, OR}^a, \text{OC(O)R}^a, \text{OC(O)NR}^a\text{R}^b, \text{NR}^a\text{R}^b, \text{NR}^a\text{C(O)R}^b, \text{NR}^a\text{S(O)}_2\text{R}^b, \text{NR}^a\text{C(O)NR}^b\text{R}^c, \text{NR}^a\text{C(S)NR}^b\text{R}^c, \text{NR}^a\text{C(NR}^b)\text{NR}^c\text{R}^d, \text{NR}^a\text{C(O)OR}^b,} \\ \text{S(O)NR}^a\text{R}^b, \text{S(O)}_2\text{NR}^a\text{R}^b, \text{S(O)}_2\text{R}^a, \text{S(O)}_2\text{R}^a, \text{C(O)OR}^a, \text{C(O)OR}^a, \text{or C(O)NR}^a\text{R}^b;} \\ \end{array}$ 

R<sub>5</sub> is H or alkyl;

n is 0, 1, 2, 3, 4, 5, or 6;

A is O, S, S(O), S(O)<sub>2</sub>, or  $NR^e$ ;

B is N or CR<sup>f</sup>;

X is O, S, S(O), S(O)<sub>2</sub>, NR<sup>e</sup>, or C(O);

Y is a covalent bond, C(O), C=NRa, O, S, S(O), S(O)2, or NRe;

Z is N or CH;

each of U and V, independently, is N or CR; and

W is O, S, or NRe;

in which each of  $R^a$ ,  $R^b$ ,  $R^c$ , and  $R^d$ , independently, is H, alkyl, aryl, heteroaryl, cyclyl, or heterocyclyl;  $R^e$  is H, alkyl, aryl, acyl, or sufonyl; and  $R^f$  is H, alkyl, aryl, acyl, sulfonyl, alkoxyl, amino, ester, amide, CN, or halogen.

54. A composition comprising an effective amount of a compound of formula (I"):

$$R_3$$
 $R_4$ 
 $R_4$ 
 $R_5$ 
 $R_5$ 
 $R_1$ 

wherein

R<sub>1</sub> is anyl or heteroaryl;

each of R<sub>2</sub> and R<sub>4</sub>, independently, is H, halogen, CN, alkyl, OR<sup>a</sup>, or NR<sup>a</sup>R<sup>b</sup>;

R<sub>3</sub> is H, halogen, CN, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cyclyl, heterocyclyl, OR<sup>a</sup>, OC(O)R<sup>a</sup>, OC(O)NR<sup>a</sup>R<sup>b</sup>, NR<sup>a</sup>R<sup>b</sup>, NR<sup>a</sup>C(O)R<sup>b</sup>, NR<sup>a</sup>S(O)R<sup>b</sup>, NR<sup>a</sup>C(O)NR<sup>b</sup>R<sup>c</sup>, NR<sup>a</sup>C(S)NR<sup>b</sup>R<sup>c</sup>, NR<sup>a</sup>C(NR<sup>b</sup>)NR<sup>c</sup>R<sup>d</sup>, NR<sup>a</sup>C(O)OR<sup>b</sup>, S(O)R<sup>a</sup>R<sup>b</sup>, S(O)<sub>2</sub>NR<sup>a</sup>R<sup>b</sup>, S(O)<sub>2</sub>R<sup>a</sup>, S(O)<sub>2</sub>R<sup>a</sup>, C(O)R<sup>a</sup>, or C(O)NR<sup>a</sup>R<sup>b</sup>;

R<sub>5</sub> is H or alkyl;

n is 0, 1, 2, 3, 4, 5, or 6;

A is O, S, S(O), S(O)<sub>2</sub>, or  $NR^e$ ;

B is N or CRf;

X is O, S, S(O), S(O)<sub>2</sub>,  $NR^e$ , or C(O);

Y is a covalent bond, C(O), C=NRa, O, S, S(O), S(O)2, or NRe;

Z is N or CH;

each of U and V, independently, is N or CR; and

W is O, S, or NRe;

in which each of R<sup>a</sup>, R<sup>b</sup>, R<sup>c</sup>, and R<sup>d</sup>, independently, is H, alkyl, aryl, heteroaryl, cyclyl, or heterocyclyl; R<sup>e</sup> is H, alkyl, aryl, acyl, or sufonyl; and R<sup>f</sup> is H, alkyl, aryl, acyl, sulfonyl, alkoxyl, amino, ester, amide, CN, or halogen

or a pharmaceutically acceptable salt, solvate, clathrate, or prodrug thereof.

- 55. A method for treating or preventing a disorder associated with excessive bone loss, the method comprising administering to a patient in need thereof a compound according to claim 49 or 52, a composition comprising an effective amount of a compound according to claim 49 or 52, a compound according to formula (I') or (I") as described in any one of claims 50 or 53, or a composition according to any one of claims 51 or 54.
- 56. The method according to claim 55, wherein the disorder is selected from the group consisting of periodontal disease, non-malignant bone disorders (such as osteoporosis, Paget's disease of bone, osteogenesis imperfecta, fibrous dysplasia, and primary hyperparathyroidism) estrogen deficiency, inflammatory bone loss, bone malignancy, arthritis, osteopetrosis, and certain cancer-related disorders (such as hypercalcemia of malignancy (HCM), osteolytic bone lesions of multiple myeloma and osteolytic bone metastases of breast cancer and other metastatic cancers).
- 57. A method for inhibiting osteoclast formation in a pre-osteoclast cell the method comprising contacting the cell with a compound according to claim 49 or 52, a composition comprising an effective amount of a compound according to

claim 49 or 52, a compound according to formula (I') or (I") as described in any one of claims 50 or 53, or a composition according to any one of claims 51 or 54.